

Prophylactic surgery prior to extended-duration space flight: Is the benefit worth the risk?

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This article explores the potential benefits and defined risks associated with prophylactic surgical procedures for astronauts before extended-duration space flight. This includes, but is not limited to, appendectomy and cholecystectomy. Furthermore, discussion of treatment during space flight, potential impact of an acute illness on a defined mission and the ethical issues surrounding this concept are debated in detail.

Cet article explore les avantages possibles et les risques définis associés à des interventions chirurgicales prophylactiques (notamment appendicectomie et cholécystectomie) chez les astronautes devant effectuer des séjours prolongés dans l'espace. Le traitement pendant le séjour dans l'espace, les répercussions éventuelles d'une maladie grave au cours d'une mission particulière et les enjeux éthiques entourant la question y sont débattus en profondeur.

The potential to regularly extend human space flight beyond low-earth orbit is current. In the coming years, the National Aeronautics and Space Administration (NASA) in the United States and similar programs in other countries expect to return to the moon with the anticipation of lunar inhabitance.¹ Furthermore, a move toward the human exploration of Mars is in the planning stages.¹ Private industry is also rapidly developing space-faring technology and hardware.

Exploration has always been associated with a substantial human cost.^{2,3} Space exploration is no exception, as illness and injury have been responsible for more mission delays and failures than either defective transport engineering or weather-related issues.⁴ In addition to traumatic injury (ranked at the highest level of concern regarding the probable incidence v. impact on mission and crew member health),⁵ other life-threatening emergency surgical conditions may arise without prior warning in even the healthiest crew members.^{6,7} These conditions include, but are not limited to, appendicitis, cholecystitis, diverticulitis, pancreatitis, peptic ulcer disease and intestinal obstruction.

Whereas numerous studies performed in the context of parabolic flight suggest that surgery in a weightless environment would be technically possible, substantial challenges remain.^{8–15} Given both equipment and manpower constraints, the challenges include restricted perioperative imaging capabilities, limited availability of surgical equipment owing to payload weight constraints, nonsurgeon crew medical officers (CMOs) with limited medical training, and potential inability to provide basic perioperative or postoperative anesthesia or nursing and rehabilitation care.^{16–18} These expected limitations do not begin to address the potential need for critical care support of a crew member with a surgical emergency.^{4,17–20} In addition to the inherent hostility of their environment, CMOs and flight surgeons must also consider the potential impact on mission objectives when assessing a crew's response to an ill crew member. Unlike the past “scoop and run” strategy that required only stabilization and rapid evacuation, the reality of a “stand and fight” scenario is much more involved.²¹ With missions of increasing duration and distance, accurate in-flight diagnosis and treatment will become more crucial. The time to definitive

medical/surgical care will also become much longer. This will undoubtedly describe the scenario during an expedition to Mars. The situation confronting a lunar base mission is also interesting in that even though the time to definitive medical care back on earth (4 d) has greatly increased (compared with shuttle [6 h] or International Space Station missions [24 h]), the capabilities of the available medical care system are not substantially different from those found on the shuttle (medical kit weight restriction is 40 lbs). This may actually result in an increased lunar medical/surgical risk. The complexity of this issue is substantial considering the impact of either a false-positive (hundreds of millions of dollars in lost mission objectives) or false-negative (protracted course of illness and risk of complications) diagnosis. As a result, the importance of identifying astronauts who are potentially predisposed to these conditions and revisiting all medical avenues to reduce risk has been re-emphasized.²²

Although the list of potential nontrauma surgical emergencies is extensive, diseases of the appendix and gallbladder (appendicitis and cholecystitis) are common and unified by our ability to prophylactically remove these organs before space flight. Prophylactic surgical excision also has a negligible effect on the function and overall health of a patient. This review discusses the predicted risk of appendicitis and cholecystitis during extended-duration expeditions and the potential role for prophylactic appendectomy and cholecystectomy.

RISK OF ACUTE APPENDICITIS

Acute appendicitis is considered a surgical emergency. Although its global incidence is decreasing, appendicitis occurs in up to 1 in 7 individuals.^{23,24} The risk of appendicitis also decreases with age. More specifically, it is estimated to range from 3.7 per 1 million person-days among individuals aged 30–34 years to 1.8 per 1 million person-days among those aged 50–54 years.⁴ As a result, the age of a given crew member may be particularly important; the ages of recent International Space Station inhabitants ranged from 30 to 56 years. Although an actual case of acute appendicitis has not been formally documented during space flight,²⁵ the Russian space program has had the most practical experience with possible cases. Specifically, acute appendicitis was suspected in a Salyut 7 cosmonaut (1985) when he initially experienced severe right lower quadrant abdominal pain. Medical evacuation was considered and preparations were initiated for an immediate recovery; however, both were avoided when it became apparent he had ureterolithiasis. Unfortunately, evacuation from Salyut was completed in 1982 when an ill cosmonaut was also suspected to have appendicitis. Prostatitis was diagnosed after his return to earth.⁴

The true risk of acute appendicitis during extended-duration space flight is unknown. As a result, predicted risk

must be generated from our closest environmental analogues. These include Russian space station, naval submarine and multinational Antarctic expeditions. Using these analogues, the risk of appendicitis has been reported to be as high as 43 per 1 million person-days (Australian Antarctic program).²⁶ This risk of 1 case every 10.6 years (9.4%/yr) is substantially higher than the 1 case every 125 years (0.8%/yr) calculated for a 6-member crew employing U.S. general population data.⁴ Furthermore, the Australian Antarctic program has reported 1 death and a 40% perioperative complication rate associated with appendicitis over a 32-year experience.

Also unclear is the impact of alterations in human physiology and anatomy that are known to occur during space flight on the incidence, presentation and natural history of appendicitis.^{4,16,27,28} For example, the manifestations of appendicitis could potentially differ between the zero-gravity phase of flight (i.e., change in the anatomic location of an inflamed appendix similar to that observed during pregnancy) and the partial gravitational environments associated with planetary destinations (i.e., comparative manifestations to earth). Similar concerns exist for the ability of a crew member to accommodate for and recover from the hemodynamics and volume status changes associated with weightlessness.^{27,28} The relative effects of immunosuppression have also been suggested as causes of the increased rates of appendicitis and its atypical presentation in Antarctica.^{29–32} Although altered immunological response and possible changes in bacterial virulence are believed to occur during space flight,^{33–35} the effect of these changes on surgical inflammatory emergencies, such as appendicitis, is unknown.

RISK OF CHOLECYSTITIS

The true risk of acute or chronic cholecystitis during an extended-duration expedition is also unknown. Fortunately, there has yet to be a reported case of symptomatic gallbladder disease during space flight. This may be related to reduced risk in the astronaut population owing to a lower average body mass index than that in the general population and to intensive medical screening at the time of selection and yearly recertification. Although the incidence of gallstones in the general population varies from 10% to 20%,³⁶ the risk of progression to symptomatic disease is about 1%–4% per year.³⁷ Because this risk is relatively low, affecting less than one-third of people over their lifetime,³⁷ expectant management for asymptomatic cholelithiasis is considered the standard of care.³⁸ Interestingly, in patient populations at increased risk for gallstones (e.g., bariatric obesity surgery, hereditary spherocytosis populations, solid organ transplant recipients), symptomatic progression of gallstones and/or increased morbidity associated with the subsequent treatment of acute cholecystitis, “routine” prophylactic cholecystectomy has been strongly

advocated.^{39–41} More specifically, transplant-related immunosuppression and the resultant heightened risk of gallbladder-associated infectious morbidity and mortality are thought to be particularly important.⁴² As previously mentioned, the impact of space flight–induced immunosuppression on a potential episode of cholecystitis is unclear. The effect of altered human physiology on gallstone formation (cholesterol/lipid biochemistry and relative hypovolemia) and gallbladder function (contractility and absorption) is also unknown. Furthermore, although the specific risk of biliary stone/sludge–induced pancreatitis during space flight remains undefined, its occurrence is plausible given the global delay of gastrointestinal function observed in microgravity.

TREATMENT OF ACUTE APPENDICITIS AND CHOLECYSTITIS

The current standard of care for uncomplicated acute appendicitis and cholecystitis is laparoscopic removal of the inflamed organ. If a minimally invasive approach is not possible, open procedures are considered the gold standard. Laparoscopic appendectomy for uncomplicated appendicitis has been shown to be better than^{43–48} or as good as⁴⁹ open appendectomy in terms of postoperative wound infections, analgesia requirements, length of stay in hospital, return to work intervals and overall recovery. In cases of complicated appendicitis (perforation or intra-abdominal abscess), the laparoscopic technique has also been shown to be superior to open procedures with regards to wound infections, postoperative intra-abdominal abscesses, hematomas and hemorrhage.^{43,50}

Whereas the minimally invasive surgical technique is currently the primary method of treatment for both appendicitis and cholecystitis, nonoperative treatment of both disease processes is not uncommon. More specifically, nonoperative therapies (bowel rest, intravenous fluids, nasogastric decompression, antibiotics) have often been required in remote medical care situations with poor surgical capabilities.⁴ Whether limited by surgical equipment or human training, most reported nonoperative cases have had good results.^{4,51–56} These include a particularly long history aboard naval submarines with success rates approaching 90%.^{4,57}

Unlike appendicitis, cholecystitis is much more commonly managed nonoperatively. Depending on the duration of symptoms at the time of presentation (delayed), many patients are initially treated without a cholecystectomy. Intravenous antibiotics, chemical analgesia and rehydration become primary therapies. These patients then typically undergo a subsequent cholecystectomy on an elective basis.

It should also be noted that in cases of periappendiceal abscess/perforation and acute cholecystitis in nonoperative candidates, image-guided percutaneous insertion of drainage catheters is a viable option. This technique has a high

success rate (> 90%) and is commonly employed in terrestrial hospitals.^{58–62} The actual act of percutaneous aspiration of intra-abdominal fluid collections has also been shown to be possible in weightlessness.⁶³ Assuming one could avoid contaminating the spacecraft and securely dispose of the biologic waste, catheter drainage is a plausible option for crew members with access to ultrasonography for image guidance. Image-guided robotic systems have also been successfully employed in interventional radiology suites and suggest that “smart” medical systems might assist CMOs in catheter insertion during long space missions in the future.^{64–66} Percutaneous catheter drainage is also common for abscesses caused by perforated viscus (inflammatory bowel disease, diverticulitis).⁶⁷

PREVENTION OF ACUTE APPENDICITIS AND CHOLECYSTITIS

Given the immense logistical, training and perioperative risks associated with the potential treatment of either appendicitis or cholecystitis during extended-duration space exploration, the concepts of prophylactic appendectomy and/or cholecystectomy should be considered. Evaluation of the true utility of this concept requires an accurate assessment of the probability that either condition will develop and cause harm. This is then compared with the risk of performing prophylactic organ removal before embarking on an expedition. As previously mentioned, however, the true risk of acute appendicitis and cholecystitis occurring in weightlessness during an extended-duration mission remains unclear. This arguably supports prophylactic organ removal to prevent the theoretical catastrophic loss of mission and/or human life in the unpredictable environment of extended-duration space flight. It should be noted that a Mars mission would entail a 2- to 4-year voyage with an estimated evacuation time of 9 to 12 months.^{25,68–70} Delayed electronic signal transmissions of up to 50 minutes would also make both communication and real-time robotic surgery and/or telementoring nearly impossible.^{25,63} Until autonomous (closed-loop) image-guided smart medical systems are developed and installed on spacecraft,^{71–73} risk management via the prevention of these acute circumstances remains a plausible and important concept.

Owing to the perceived increased risk of acute appendicitis during Antarctic expeditions, prophylactic appendectomy for those spending the winter has been mandatory in the Australian program since 1950.²⁶ Whereas prophylactic removal of the appendix has been avoided for U.S. explorers, Russia, United Kingdom, France, Chile and Argentina have each used this policy intermittently.⁴ Because of its relatively reduced risk, there is no report of routine prophylactic cholecystectomy for Antarctic, submarine or space flight expeditions.

The risks associated with laparoscopic surgery to remove the appendix in a noninflamed state are poorly studied.

Risks for any minimally invasive procedure include the general risks of the anesthetic itself (1 in 250 000 for a trained anesthesiologist in optimal conditions), hemorrhage, wound infection and unrecognized gastrointestinal perforation. Appendectomy-specific risk primarily involves leakage from the occluded base of the appendix (staple line, suture or tie) and small bowel obstruction secondary to postoperative adhesions. Although the subsequent risk of a small bowel obstruction is small (0.0069 cases per person-year),⁷⁴ the potential impact of this complication during space flight is substantial given limited on-board medical resources (intravenous fluids). Risks for a prophylactic cholecystectomy are much better studied. These include the same general risks as a laparoscopic appendectomy, but also the potential of a bile duct injury and significant hemorrhage from the liver (gallbladder bed/cystic plate). Bile duct injuries are life-altering in terms of both patient outcome and recovery.⁷⁵ They occur at a rate of 0.4% in the nearly 700 000 cholecystectomies (90% laparoscopic) performed each year in the United States.⁷⁶⁻⁷⁸ This compares to an injury rate of 0.2% among open cholecystectomies.⁷⁹ The incidence of significant hemorrhage during laparoscopic cholecystectomy ranges from 0.1% to 1.9%,^{80,81} with most of the bleeding originating from a relatively common superficial branch of the middle hepatic vein.⁸²

Although reports outlining the safety of concurrent prophylactic laparoscopic procedures (cholecystectomy and appendectomy) are limited, a small prospective controlled study of simultaneous open appendectomy and cholecystectomy deemed combined procedures to have no increased risk.⁸³ Furthermore, simultaneous laparoscopic cholecystectomy with either a splenectomy⁴¹ or Roux-en-Y gastric bypass⁴⁰ have also been shown to be safe. Given that these additional procedures are considered to be more difficult than an appendectomy, extrapolation of safety to a concurrent appendectomy/cholecystectomy appears reasonable.

It should be noted that although additional nontrauma surgical emergencies are plausible in astronauts on extended-duration expeditions, they are either not appropriate for prophylactic laparoscopic procedures (peptic ulcer disease, intestinal obstruction, pancreatitis) or have near-normal population risks of advancing to acute pathological states, assuming patients have not been previously symptomatic (Meckel diverticulum, sigmoid diverticulosis).⁸⁴ The exception is biliary stone/sludge-induced pancreatitis. Prophylactic removal of the gallbladder would also eliminate this risk.

OTHER MINIMALLY INVASIVE OPTIONS FOR SURGICAL PROPHYLAXIS

Single-incision laparoscopic operations have recently emerged as a potentially viable alternative to standard laparoscopy.⁸⁵ Unlike traditional laparoscopy, which requires multiple incisions, this technique uses multiple ports

through a single incision. Whereas postoperative benefits may theoretically include reduced postoperative pain, wound complications and convalescence, obvious advantages include improved cosmesis and greater patient satisfaction. As a result, this technique has recently been applied to a large array of procedures, including cholecystectomy,⁸⁶⁻⁸⁹ appendectomy,⁹⁰ colectomy⁹¹ and donor nephrectomy⁹² among others. Unfortunately with the current generation of single-incision laparoscopic instruments, this procedure is clearly more difficult for many surgeons than traditional laparoscopic surgery. Increased duration of surgery, a common need for extra skin incisions and a trend toward more incisional pain are often reported.⁸⁵ There is also a lingering concern of potential increases in the rate of common bile duct injuries during the early learning curve for this technique. Whereas more research is needed to fine-tune this technique and prove both the safety and unique benefits of the concept, continued development of improved instrumentation (larger single-port working platforms, flexible fulcrum instruments, multiplane optical sources) is encouraging.⁸⁵

Natural orifice transluminal endoscopic surgery (NOTES), now in clinical trials in the United States, may represent another modality compatible with space exploration for various surgical conditions.⁹³ This procedure involves the intentional puncture of a viscera (stomach, urinary bladder, rectum, vagina) with an endoscope to enter the peritoneal cavity and complete the required operative procedure.⁹⁴ Both appendices and gallbladders have been removed via this approach. The total absence of an incision (the expected future for NOTES) may make prophylactic removal of the appendix and/or the gallbladder more palatable. The NOTES technique would also mitigate management of incisional and peritoneal fluid in an altered gravity environment. The already closed nature of the peritoneal cavity provides a natural containment for blood and fluid. Whereas the specific effects of weightlessness on NOTES-related organs and endoscopes are currently unknown, there are likely to be additional unanticipated challenges if employed during space exploration. Although the predicted benefits of this technique echo those for single-incision laparoscopic procedures,⁹⁵⁻⁹⁷ cautious safety and feasibility studies must precede widespread adoption of this technique for the extended-duration space-faring population.

ETHICAL ISSUES

Whereas there is reasonable evidence to support the concept of prophylactic appendectomy and cholecystectomy before embarking on an extended-duration space mission, the ethics of removing healthy organs to prevent a possible future complication in a healthy crew member must be discussed. In a large space coalition, all partner countries would presumably need to agree and participate. Furthermore, the personal consequences of an operative complication after

prophylactic organ removal might be substantial (e.g., disqualification from flight). As a result, it is unclear whether this strategy would be mandatory, or simply based on a crew decision with informed consent regarding personal and mission risk (similar to patent foramen ovale screening). The financial cost of the procedure, and of any subsequent complications, would also have to be addressed.⁹⁸ As Jennings and colleagues have noted,^{99,100} the ethical considerations of exposing individuals with pre-existing medical conditions to prophylactic surgical procedures and at-risk testing before space flight present novel challenges. These become particularly complicated when clinicians (providing diagnostic and therapeutic services) and space-related medical boards (defining medical requirements for certification and space flight) do not agree.

If prophylactic surgery was required prior to consideration for selection for an expedition, the procedure and its associated medical risks would have to be balanced against an unclear potential benefit. Prophylactic surgery might be considered an advantage for an astronaut who was being considered for, but not guaranteed, a spot on a flight. If prophylactic surgery became mandatory after astronaut selection for a given mission, then an individual would have no choice but to undergo the procedure or be deselected. This person would therefore be allowed minimal freedom of choice with enormous peer, corporate and even public pressure to comply.

There are numerous methods of enhancing human performance. For space flight in particular, the most important tools remain selection, training, equipment, pharmacology and surgery. The specific modalities available for each range from ethically acceptable to unacceptable. Even when someone consents to a particular procedure aimed at enhancing performance, this action may be ethically unacceptable to society as a whole. The burden of risk for the individuals themselves may also be too great. Furthermore, several characteristics define the acceptability of consent. Each method of enhancing performance should be examined in the context of the principles of medical ethics in a relevant society. These are defined as autonomy, nonmaleficence, beneficence and justice. Only then can we develop a morally justifiable code of practice that balances society's needs against individual ambitions and corporate goals.⁹⁸

CONCLUSION

The theoretical incidence of acute appendicitis and cholecystitis during an extended-duration exploration could be increased. The impact of altered human physiology, anatomy and immunology during space flight on the natural history and clinical course of either disease is unknown. As a result of the immense potential risk for loss of mission and/or human life, however, prophylactic surgical removal of a crew member's healthy appendix should be considered. This may also apply to a healthy gallbladder

despite the low risk of cholecystitis in the absence of gallstones. Finally, the presence of gallstones clearly represents the greatest threat. There is a recognized, albeit minimal, risk of perioperative and postoperative complications from prophylactic organ excision. Given these small risks in this healthy patient population, the limited number of candidates and continually advancing minimally invasive surgical options, the ease and safety of surgical prophylaxis currently appears to outweigh the logistics of treating either acute appendicitis or cholecystitis during extended-duration space flight.

Because the time to reach definitive medical care on earth will be extremely long, and rescue or medical evacuation likely unavailable, future extended-duration space flights (e.g., Mars expedition) would ideally include a medical care system with greater surgical capability. Increased limitations on surgical care expected in extended-duration missions necessitate a surgically capable CMO and an advanced life support system. Whereas focusing on the specific incidences of individual surgical events (i.e., appendicitis and potentially cholecystitis) does not necessarily justify increased surgical capability, the potential incidence of "any and all" surgical problems occurring during space flight does. As a result, we advocate more extensive surgical capabilities for future extended-duration space flight medical care systems owing to the increased risk of various surgical events (including appendicitis and cholecystitis in nonprophylaxed patients). If it is not possible to provide level 4 (limited surgical) and level 5 (major surgical) care on either the moon or Mars, however, prophylactic excisional surgery is a reasonable alternative in spite of the extensive unresolved ethical issues associated.

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